AMR research in a post-pandemic world: Insights on antimicrobial resistance research in the COVID-19 pandemic

Jesús Rodríguez-Baño, Gian Maria Rossolini, Constance Schultsz, Evelina Tacconelli, Srinivas Murthy, Norio Ohmagari, Alison Holmes, Till Bachmann, Herman Goossens, Rafael Canton, Adam P. Roberts, Birgitta Henriques-Normark, Cornelius J. Clancy, Benedikt Huttner, Patriq Fagerstedt, Shawon Lahiri, Charu Kaushic, Steven J. Hoffman, Margo Warren, Ghada Zoubiane, Sabiha Essack, Ramanan Laxminarayan, Laura Plant

PII: S2213-7165(21)00045-X

DOI: https://doi.org/10.1016/j.jgar.2021.02.013

Reference: JGAR 1496

To appear in: *Journal of Global Antimicrobial Resistance*

Received Date: 15 January 2021

Accepted Date: 16 February 2021

Please cite this article as: Rodríguez-Baño J, Rossolini GM, Schultsz C, Tacconelli E, Murthy S, Ohmagari N, Holmes A, Bachmann T, Goossens H, Canton R, Roberts AP, Henriques-Normark B, Clancy CJ, Huttner B, Fagerstedt P, Lahiri S, Kaushic C, Hoffman SJ, Warren M, Zoubiane G, Essack S, Laxminarayan R, Plant L, AMR research in a post-pandemic world: Insights on antimicrobial resistance research in the COVID-19 pandemic, *Journal of Global Antimicrobial Resistance* (2021), doi: https://doi.org/10.1016/j.jgar.2021.02.013

AMR research in a post-pandemic world: Insights on antimicrobial resistance research in the COVID-19 pandemic

Short title: Insights on antimicrobial resistance research in the COVID-19 pandemic

Jesús Rodríguez-Baño[1 2 3], Gian Maria Rossolini[4 5], Constance Schultsz[6], Evelina Tacconelli[7], Srinivas Murthy[8], Norio Ohmagari[9], Alison Holmes[10], Till Bachmann[11], Herman Goossens[12], Rafael Canton[13 14], Adam P. Roberts[15], Birgitta Henriques-Normark[16 17], Cornelius J. Clancy[18], Benedikt Huttner[19], Patriq Fagerstedt[20], Shawon Lahiri[20], Charu Kaushic[21 22], Steven J. Hoffman[23], Margo Warren[24], Ghada Zoubiane[25], Sabiha Essack[25 26], Ramanan Laxminarayan[27], Laura Plant*[21]

[1]Unidad Clínica de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen Macarena, Sevilla, Spain.

[2]Departamento de Medicina, Universidad de Sevilla, Sevilla, Spain.

[3]Instituto de Biomedicina de Sevilla (IBiS), Sevilla, Spain.

[4]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy.

[5]Clinical Microbiology and Virology Unit, Florence Careggi University Hospital, Florence, Italy.

[6]Department of Global Health - AIGHD Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands.

[7]Division of Infectious Diseases, Department of Diagnostic and Public Health, University of Verona, Verona, Italy

[8]BC Children's Hospital, University of British Columbia, Vancouver, Canada.

[9]Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan.

[10]Department of Medicine, Faculty of Medicine, Imperial College London, London, UK.

[11]The University of Edinburgh, Edinburgh Medical School, Division of Infection and Pathway Medicine, The Chancellor's Building, Edinburgh, UK.

[12]Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium.

[13]Servicio de Microbiología. Hospital Universitario Ramón y Cajal and Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain.

[14]Red Española de Investigación en Patología Infecciosa (REIPI). Instituto de Salud Carlos III. Madrid, Spain.

[15]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK.

[16]Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden.

[17]Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden.

[18]University of Pittsburgh. 3550 Terrace St. Scaife Hall 867. Pittsburgh, USA.

[19]Division of Infectious Diseases, Geneva, University Hospitals; Faculty of Medicine, University of Geneva, Geneva, Switzerland.

[20]JPIAMR Secretariat, Swedish Research Council, Stockholm, Sweden.

[21]Institute of Infection and Immunity, Canadian Institutes of Health Research

[22]McMaster Immunology Research Center, Dept Pathology and Mol. Medicine, McMaster University, Hamilton, ON, Canada

[23]Global Strategy Lab, Dahdaleh Institute for Global Health Research, Faculty of Health and Osgoode Hall Law School, York University, Toronto, M3J 1P3, Canada

[24]Access to Medicine Foundation, Naritaweg 227-A, 1043 CB, Amsterdam, The Netherlands.

[25]International Centre for Antimicrobial Resistance Solutions (ICARS), Copenhagen, Denmark

[26]Antimicrobial Research Unit, University of KwaZulu-Natal, Durban, South Africa.

[27]Center for Disease Dynamics, Economics & Policy, New Delhi India.

[*]Corresponding Author: Laura Plant, JPIAMR Secretariat

Swedish Research Council

Box 1035, 101 38 Stockholm

Telephone: +46 (0) 733 1026 79

Email: Laura.Plant@vr.se

Highlights:

- Antibiotics were excessively used in hospitalised COVID-19 patients.
- COVID-19 caused major disruptions to AMR surveillance and research.
- Global data on the use of antibiotics during the COVID-19 pandemic is needed.
- Antimicrobial resistance needs continued public and political engagement.

The COVID-19 pandemic is predicted to impact the transmission of bacterial infections and the emergence of antibiotic resistance (AMR). The likely positive influence on antibiotic resistance that social distancing, increased awareness and the use of interventions to prevent the transmission of COVID-19 has had could also be counteracted by the reported excessive use of broad spectrum antibiotics to treat patients infected with SARS-CoV-2. Antimicrobial stewardship programmes and AMR focussed research activities must remain active during

the COVID-19 and future pandemics, in order to safeguard against an uncontrolled rise in AMR.

Antibiotic use in the COVID-19 pandemic

The priority during the COVID-19 pandemic has been treating patients and avoiding acquisition of SARS-CoV-2 by healthcare personnel whilst maintaining functionality of the healthcare systems. Within healthcare, there has been a need to redirect personnel, resources and attention to COVID-19 diagnosis and management. AMR surveillance and screening programmes to detect colonisation by resistant organisms have been compromised due to shortage of personnel and the need to redirect molecular diagnostic platforms, reagents, tracking and tracing from AMR surveillance to COVID-19 diagnostics.

It has been reported that only 7-8% of hospitalised COVID-19 patients were diagnosed with a bacterial or fungal infection [1, 2, 3], while antibiotic use in COVID-19 patients has been considerably high: 71.9% (95% CI: 56.1-87.7) [3]. Further studies using molecular techniques on samples from ventilated and non-ventilated COVID-19 patients are needed. Whether new or evolving AMR in COVID-19 patients will emerge in areas with low previous rates should be examined in retrospective and prospective clinical and microbiology studies.

Simultaneously managing the acute COVID-19 pandemic and escalating AMR

COVID-19 has illustrated the vulnerability of our healthcare systems. This is even more noticeable in Low and Middle Income Countries (LMICs) and in resource-constrained settings less prepared to deal with pandemics or other emergencies [4-6]. Local, national and international scale resistance data is needed to help researchers better understand potential disruptions in stewardship and surveillance efforts, and highlight the early emergence of resistance due to antibiotic use linked to COVID-19 and secondary infections.

Co-managing multiple infectious disease threats simultaneously is a further challenge for LMICs. Laboratory infrastructure, surveillance and diagnostic capacity for both COVID-19

and AMR are often unreliable and infection prevention and control policies, practice and personnel are sub-optimal and, or, unsustainable [7]. Regulated antibiotic use is difficult to enforce where there is poor access to antibiotics overall, while socio-behavioural interventions such as physical distancing and hand hygiene can be limited, especially in areas with high population densities with limited access to clean water and sanitation services Thus, an exit strategy from COVID-19 for many LMICs may not be pharmacologically based in the short term and more community-based strategies are currently being explored [8].

Impact of the COVID-19 pandemic on AMR research

A critical lesson from the COVID-19 pandemic is the importance of embedding research in the response. Supporting good quality implementation research could help understand not only what has worked, but also how and why an intervention was successful. While research on COVID-19 due to the pandemic has progressed, research in other fields including AMR has been deprioritised, delayed, or even halted. Delays limit scientists to meet deadlines and targets within projects, and restrict sharing of information and networking activities. Funding agencies across the globe have given research grant extensions; however, the long-term impact on AMR research is yet to be understood and factors such as the effect on early career researchers may take years to manifest. As solidarity pledges emerge to address COVID-19, so too must efforts to openly share research and data ’on AMR, including surveillance data from the pharmaceutical industry, as incentivised by the Access to Medicine Foundation’s AMR Benchmark. In order to ensure that AMR research continues to be adequately supported it is important to prioritise funds for AMR research at both national and international scales.

The COVID-19 pandemic has led to an unprecedented awareness of the importance of infectious diseases, clinical microbiology, and infection control. The AMR research

community is in an ideal position to raise the awareness of the topic of AMR and build on community engagement in the importance of sanitary infrastructures [9], handwashing, disinfection, social distancing when ill, and avoiding unnecessary use of antibiotics. Harnessing the public understanding of the relevance of infectious diseases towards the long-term pandemic of AMR could have major implications for promoting good practices about control of AMR transmission.

ACKNOWLEDGEMENTS

This work was founded on the Joint Programming Initiative on Antimicrobial Resistance webinar series 'AMR in a post-pandemic world'.

CONFLICTS OF INTEREST

SE is chairperson of the Global Respiratory Partnership and member of the Global Hygiene Council both sponsored by unrestricted educational grants from Reckitt and Benckiser Ltd., UK.

FUNDING

APR would like to acknowledge funding from the AMR Cross-Council Initiative through a grant from the Medical Research Council, a Council of UK Research and Innovation (Grant Number; MR/S004793/1), the National Institute for Health Research (Grant number; NIHR200632) and the Joint Programming Initiative for Antimicrobial Resistance (JPIAMR) via the Medical Research Council in the UK (Grant number; MR/S037640/1). JRB and RC acknowledge funding on AMR from Plan Nacional de I+D+i 2013- 2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Ciencia, Innovación y Universidades, Spanish Network for Research in Infectious Diseases (REIPI RD16/0016/0001 and RD16/0016/0011), co- financed by European Development Regional Fund "A way to achieve Europe", Operative Program Intelligence Growth 2014- 2020. JRB also acknowledges Joint Programming Initiative for Antimicrobial Resistance (JPIAMR) via Instituto de Salud Carlos III (grant number: AC16/00076). ET acknowledges funding on AMR from the Joint Programming Initiative for Antimicrobial Resistance (JPIAMR) via German Federal Ministry of Education and Research (BMBF) (grant number 01KI1830), Innovative Medicines Initiative 1 and 2 Joint Undertaking (grants number 115737, 115523, 820755), and the Global Antibiotic Research and Development Partnership (GARDP).

ETHICAL APPROVAL

Not required,

REFERENCES

1. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020 May 2:ciaa530. doi: 10.1093/cid/ciaa530.

2. Langford BJ, So M, Raybardhan S, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect 2020. July 22. DOI:https://doi.org/10.1016/j.cmi.2020.07.016

3. Garcia-Vidal C, Sanjuan G, Moreno-García E, Martínez JA, Soriano A and COVID19-researchers group. Incidence of co-infections and superinfections in hospitalised patients with COVID-19: a retrospective cohort study. Clin Microbiol Infect. 30 July 2020. DOI: https://doi.org/10.1016/j.cmi.2020.07.041

4. Antimicrobial Resistance Benchmark 2020. https://accesstomedicinefoundation.org/media/uploads/downloads/5e270aa36821a_Antimicrobial_Resistance_Benchmark_2020.pdf

5. Lai CC, Wang CY, Wang YH, Hsueh SC, Ko WC, Hsueh PR. Global epidemiology of coronavirus disease 2019 (COVID-19): disease incidence, daily cumulative index, mortality, and their association with country healthcare resources and economic status. Int J Antimicrob Agents. 2020 Apr;55(4):105946. doi:10.1016/j.ijantimicag.2020.105946.

6. Bong CL, Brasher C, Chikumba E, McDougall R, Mellin-Olsen J, Enright A. The COVID-19 Pandemic: Effects on Low- and Middle-Income Countries. Anesth Analg. 2020 Jul;131(1):86-92. doi: 10.1213/ANE.0000000000004846.

7. Dubbink JH, Branco TM, Kamara KB, Bangura JS, Wehrens E, Falama AM, Goorhuis A, Jørgensen PB, Sevalie SS, Hanscheid T, Grobusch MP. COVID-19 treatment in sub-Saharan Africa: If the best is not available, the available becomes the best. Travel Med Infect Dis.

2020 Sep-Oct;37:101878. doi: 10.1016/j.tmaid.2020.101878. Epub 2020 Sep 11. PMID: 32927051; PMCID: PMC7485546.

8. Walker PGT, Whittaker C, Watson OJ, Baguelin M, Winskill P, Hamlet A, Djafaara BA, et al. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. Science. 2020 Jul 24;369(6502):413-422. doi: 10.1126/science.abc0035.

9. Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. Lancet Planet Health. 2018 Sep;2(9):e398-e405. doi: 10.1016/S2542-5196(18)30186-4.